

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1(Original). A method for detecting one or more endometrial markers or polynucleotides encoding the markers associated with an endometrial disease or an endometrium phase in a subject comprising:

- (a) obtaining a sample from a subject;
- (b) detecting in proteins extracted from the sample one or more endometrial markers or polynucleotides encoding the markers that are associated with the disease or phase; and
- (c) comparing the detected amount with an amount detected for a standard.

2(Currently Amended). A method of detecting an endometrial disease in a subject, the method comprising ~~comparing~~:

- (a) detecting the levels of one or more endometrial markers associated with endometrial disease that are extracted from a sample from the subject in accordance with the method of claim 1; and
- (b) comparing the levels in “(a)” with normal levels of expression of the endometrial markers in a control sample, wherein a significant difference in levels of endometrial markers, relative to the corresponding normal levels, is indicative of endometrial disease.

3(Currently Amended). A method as claimed in claim 1 ~~or~~ 2 comprising:

- (a) contacting a biological sample obtained from a subject with one or more binding agent that specifically binds to the endometrial markers or parts thereof; and

- (b) detecting in the sample amounts of endometrial markers that bind to the binding agents, relative to a predetermined standard or cut-off value, and therefrom determining the presence or absence of the endometrial disease in the subject.

4(Original) A method as claimed in claim 3 wherein the binding agent is an antibody.

5(Currently Amended). A method for screening a subject for endometrial cancer comprising the method of claim 1 wherein in step “(b)” the one or more endometrial markers or polynucleotides encoding the markers detected are ~~(a) obtaining a biological sample from a subject; (b) detecting in proteins extracted from the sample the amount of one or more endometrial cancer markers~~ or polynucleotides encoding same and; and (c) comparing the amount of endometrial cancer markers detected to a predetermined standard, where detection of a level of endometrial cancer markers different than that of a standard or control is indicative of endometrial cancer.

6(Original). A method of claim 5 wherein the level of endometrial cancer markers are significantly higher compared to the standard and are indicative of endometrial cancer.

7(Original). A method of claim 5 wherein the level of endometrial cancer markers are significantly lower compared to the standard and are indicative of endometrial cancer.

8(Currently Amended). A method as claimed in ~~any preceding~~ claim 5 wherein the sample is obtained from tissues, extracts, cell cultures, cell lysates, lavage fluid, or physiological fluids.

9(Original). A method as claimed in claim 8 wherein the sample is obtained from a tumor tissue.

10(Currently Amended). A method as claimed in ~~any preceding~~ claim 5 which further comprises detecting multiple cancer markers.

11(Currently Amended). A method of claim 1 for determining the presence or absence of endometrial markers associated with an endometrial disease in a subject ~~comprising detecting~~ wherein one or more polynucleotide encoding an endometrial marker in a sample is detected from the subject and relating the detected amount to the presence of an endometrial disease.

12(Original). A method as claimed in claim 11 wherein the polynucleotide detected is mRNA.

13(Original). A method of claim 12 wherein the polynucleotide is detected by

- (a) contacting the sample with oligonucleotides that hybridize to the polynucleotides; and
- (b) detecting in the sample levels of nucleic acids that hybridize to the polynucleotides relative to a predetermined standard or cut-off value, and therefrom determining the presence or absence of an endometrial disease in the subject.

14(Original). A method as claimed in claim 12 wherein the mRNA is detected using an amplification reaction.

15(Original). A method as claimed in claim 14 wherein the amplification reaction is a polymerase chain reaction employing oligonucleotide primers that hybridize to the polynucleotides, or complements of such polynucleotides.

16(Original). A method as claimed in claim 12 wherein the mRNA is detected using a hybridization technique employing oligonucleotide probes that hybridize to the polynucleotides or complements of such polynucleotides.

17(Original). A method as claimed in claim 14 wherein the mRNA is detected by (a) isolating mRNA from the sample and combining the mRNA with reagents to convert it to cDNA; (b) treating the converted cDNA with amplification reaction reagents and primers that hybridize to the polynucleotides, to produce amplification products; (d) analyzing the amplification products to detect an amount of mRNA encoding one or more endometrial markers; and (e) comparing the amount of mRNA to an amount detected against a panel of expected values for normal tissue derived using similar primers.

18(Canceled).

19(Currently Amended). A method for monitoring the progression of endometrial cancer in a subject, the method comprising: (a) detecting in a sample from the subject at a first time point, one or more endometrial cancer markers or polynucleotides encoding the markers using the method of claim 5; (b) repeating step (a) at a subsequent point in time; and (c) comparing levels detected in steps (a) and (b), and thereby monitoring the progression of endometrial cancer.

20(Currently Amended). A method for determining in a subject whether endometrial cancer has metastasized or is likely to metastasize in the future, the method comprising comparing (a) levels of one or more endometrial cancer markers or polynucleotides encoding the markers, in a subject sample in accordance with the method of claim 1; and (b) normal levels or non-metastatic levels of the endometrial cancer markers or polynucleotides encoding the markers, in a control sample wherein a significant difference between the levels of expression in the subject sample and the normal levels or non-metastatic levels is an indication that the endometrial cancer has metastasized.

21(Currently Amended). A method for assessing the aggressiveness or indolence of endometrial cancer comprising comparing: (a) levels of expression of one or more endometrial cancer markers or polynucleotides encoding the markers, in a subject sample obtained using the method of claim 1; and (b) normal levels of expression of the endometrial cancer markers or polynucleotides encoding the markers, in a control sample, wherein a significant difference between the levels in the subject sample and normal levels is an indication that the cancer is aggressive or indolent.

22(Original). A diagnostic composition comprising an agent that binds to an endometrial cancer marker or hybridizes to a polynucleotide encoding such marker.

23(Currently Amended). A method for assessing the potential efficacy of a test agent for inhibiting endometrial cancer in a subject, the method comprising: ~~comparing~~ (i) detecting in accordance with the method of claim 1: (a) levels of one or more endometrial cancer markers, in a first sample obtained from a subject and exposed to the test agent, wherein the endometrial cancer markers, ~~and~~ (b) levels of the endometrial cancer markers in a second sample obtained from the subject, wherein the sample is not exposed to the test agent, and (ii) comparing (a) and (b), wherein a significant difference in the levels of expression of the endometrial cancer markers in the first sample, relative to the second sample, is an indication that the test agent is potentially efficacious for inhibiting endometrial cancer in the subject.

24(Currently Amended). A method of assessing the efficacy of a therapy for inhibiting endometrial cancer in a subject, the method comprising comparing: (i) detecting in accordance with the method of claim 1: (a) levels of one or more endometrial cancer markers in a first sample obtained from the subject; ~~and~~ (b) levels of the endometrial cancer markers in a second sample obtained from the subject following therapy, and (ii) comparing (a) and (b), wherein a significant difference in the levels of expression of the endometrial cancer markers in the second sample, relative to the first

sample, is an indication that the therapy is efficacious for inhibiting endometrial cancer in the subject.

25(Currently Amended). A method of selecting an agent for inhibiting endometrial cancer in a subject the method comprising (a) obtaining a sample comprising cancer cells from the subject; (b) separately exposing aliquots of the sample in the presence of a plurality of test agents; (c) ~~comparing~~ detecting levels of one or more endometrial cancer markers in each of the aliquots in accordance with the method of claim 1; and (d) selecting one of the test agents which alters the levels of endometrial cancer markers in the aliquot containing that test agent, relative to other test agents.

26(Currently Amended). A method of inhibiting endometrial cancer in a subject, the method comprising (a) obtaining a sample comprising cancer cells from the subject; (b) separately maintaining aliquots of the sample in the presence of a plurality of test agents; (c) ~~comparing~~ detecting levels of one or more endometrial cancer markers in each of the aliquots in accordance with the method of claim 1 and comparing them; and (d) administering to the subject at least one of the test agents which alters the levels of endometrial cancer markers in the aliquot containing that test agent, relative to other test agents.

27(Currently Amended). A method of assessing the endometrial cancer cell carcinogenic potential of a test compound, the method comprising: (a) maintaining separate aliquots of endometrial cancer cells in the presence and absence of the test compound; and (b) ~~comparing~~ detecting the expression of one or more endometrial cancer markers, in each of the aliquots in accordance with claim 1 and comparing them, ~~and~~ wherein a significant difference in levels of endometrial cancer markers in the aliquot maintained in the presence of the test compound, relative to the aliquot maintained in the absence of the test compound, is an indication that the test compound possesses endometrial cancer cell carcinogenic potential.

28(Original). An *in vivo* method for imaging an endometrial disease comprising:

- (a) injecting a subject with one or more agent that binds to an endometrial marker, the agent carrying a label for imaging the endometrial marker;
- (b) allowing the agent to incubate *in vivo* and bind to an endometrial marker; and
- (c) detecting the presence of the label localized to diseased endometrial tissue.

29(Original). A method as claimed in claim 28 wherein the agent is an antibody that specifically reacts with an endometrial marker.

30(Currently Amended). Markers that distinguish an endometrium phase or endometrial disease identified by assaying for differential expression of polypeptides in endometrium samples in accordance with the method of claim 1.

31(Original). Markers as claimed in claim 30 wherein differential expression is assayed using mass spectroscopy of polypeptides extracted from the samples.

32(Original). Markers of claim 31 which are up-regulated in endometrial cancer.

33(Original). Markers of claim 31 which are down-regulated in endometrial cancer.

34(Original). A set of markers of claim 30 ~~or 31~~ comprising a plurality of polypeptides comprising or consisting of at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 of the markers listed in Table 1, 4, 5, or 6.

35(Original). A set of markers of claim 34 wherein the polypeptides are selected from the group consisting of polypeptides with the sequence of SEQ ID NOs. 1, 3, 6, 9, 11, 13, 15, 18, 21, 23, 30, 33, 36, 38, and 40.

36(Original). A set of markers of claim 31 wherein the polypeptides are selected from the group consisting of polypeptides with the sequence of SEQ ID NOs. 1, 3, 6, 9, 11, 13, 15, 18, 21, 23, 26, 30, 33, 36, 38, 40, 42, 45, and 47.

37(Original). A set of markers of claim 31 wherein the polypeptides are selected from the group consisting of polypeptides with the sequence of SEQ ID NOs. 26, 42, 45, and 47.

38(Currently Amended). A method of ~~any preceding~~ claim 1 wherein the endometrial markers are one or more of the polypeptides listed in Table 1 or they have a sequence of SEQ ID NOs. 1, 3, 6, 9, 11, 13, 15, 18, 21, 23, 26, 30, 33, 36, 38, 40, 42, 45, and 47.

39(Currently Amended). A method of ~~any preceding~~ claim 1 wherein the endometrial marker is chaperonin 10.

40(Canceled)

41(Original). A method of determining uterine endometrial receptivity by first obtaining a serum, uterine fluid or endometrial biopsy sample from a subject and detecting the presence of an endometrial marker associated with a certain endometrium phase, wherein the presence or absence of an endometrial marker as compared to controls indicates uterine receptivity.

42(Original). A method of claim 41 wherein the endometrium phase is the secretory or proliferative phase.

43(Currently Amended). A method of monitoring the effects of ovarian hyperstimulation and/or ovulation induction ~~protocols~~ treatments on uterine receptivity

which comprises the method of claim 41 wherein: (a) ~~obtaining a serum, uterine or fluid or endometrial biopsy~~ the sample is obtained from a subject receiving the treatments; and (b) ~~detecting wherein the certain phase in which~~ the presence of an endometrial marker is detected in the endometrium is ~~present in the endometrium~~ at the time of fertilization, early embryogenesis, and implantation; ~~wherein presence or absence of an endometrial marker indicates receptivity.~~

44(Currently Amended). A method of determining a probability of successful implantation with an ovarian stimulation *in vitro* fertilization and embryo transfer procedure, comprising detecting the uterine endometrial receptivity in accordance with the method of claim 41:

- (a) ~~determining a level of an endometrial marker in a~~ wherein the sample is obtained from a subject who has undergone an ovarian stimulation *in vitro* fertilization and embryo transfer procedure; and
- (b) wherein determining a probability of successful implantation is based on the subject's determined endometrial marker level;

wherein a significantly different endometrial marker level relative to a standard level is associated with a decreased or increased probability of successful implantation.

45(Currently Amended). A method of any of claim 41 ~~to 44~~ wherein the endometrial marker is glutamate receptor subunit zeta 1, a tryptic fragment thereof, and/or macrophage migration inhibitory factor.

46(Original). A method of contraception by interrupting the cyclic presence of an endometrial marker, in particular glutamate receptor subunit zeta 1, a tryptic fragment thereof, macrophage migration inhibitory factor, myosin light chain kinase 2, and/or tropomyosin 1 alpha chain.

47(Canceled).

48(Original). A kit for determining the presence of an endometrial disease in a subject, comprising a known amount of one or more binding agent that specifically binds to an endometrial marker wherein the binding agent comprises a detectable substance, or it binds directly or indirectly to a detectable substance.

49(Currently Amended). A kit for determining the presence of endometrial disease in a subject of claim 48 wherein the binding agent is, ~~comprising a known amount of an~~ oligonucleotide that hybridizes to a polynucleotide encoding an endometrial marker wherein the oligonucleotide is directly or indirectly labeled with a detectable substance.